

Yellow Urticaria in a patient with gallbladder stones: A case report and review of literature

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ABSTRACT

Yellow urticaria is a rare type of urticaria and the exact etiology behind it is still unclear. We report a case of 53-years-old medically free male with pruritic yellow to orange wheals over his trunk and extremities after receiving his first dose of COVID-19 Vaccine (Pfizer-BioNTech) with no evidence of angioedema or anaphylaxis. All the reported cases of yellow urticaria almost share the same cause which is hyperbilirubinemia due to wide spectrum of liver diseases. In conclusion, it is crucial for clinicians to be familiar with this presentation of yellow urticaria and correlate it with the patient history related to liver disease, as this urticaria often signifies the presence of various liver disorders.

Keywords: Yellow Urticaria, bilirubin, gallbladder stones, hyperbilirubinemia

1. INTRODUCTION

Urticaria, which is also known as hives, is a heterogeneous group of disorders that share a distinct skin reaction pattern. Urticaria typically, presents as well-circumscribed, erythematous, intensely pruritic plaques that last for less than 24 hours (Zuberbier et al., 2014). The lesions may be round, polymorphic, or serpiginous, and can rapidly grow and coalesce (Zuberbier et al., 2014). The underlying etiology of urticaria could be Immunoglobulin E (IgE) mediated, Non-IgE immunologically mediated or non-immunologically mediated (Schaefer, 2017). Yellow urticaria is an uncommon variant of urticaria which is infrequently discussed and reported in literature. The common cause between the reported cases of yellow urticaria is hyperbilirubinemia which is encountered in patients with infective hepatitis, liver cirrhosis or biliary diseases (Boechat Souza et al., 2017). We describe a rare case of yellow urticaria in a patient with gallbladder stones.

2. CASE

A 53-year-old male has visited the clinic complaining of itchy rash at different parts of his body during the last month. The problem started 2 weeks after



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receiving his first dose of COVID-19 Vaccine (Pfizer-BioNTech) as red, warm and itchy swellings at his thighs, arms and the abdomen. The rash usually lasts for a long time then disappears without residual changes to re-appear at other sites of the body. There was no swelling of his lips or eyelids, shortness of breathing or joint pain. He was seen by a dermatologist and was prescribed topical steroids and oral antihistamine that provided temporary relief. The patient has no history of any chronic diseases and not on any medications at the visit time.

On examination, the vital signs were normal and the patient was not in distress. There were multiple wheals mainly at the inner aspect of the thighs, outer aspects of the arms and the trunk (Figure 1). The wheals were yellow to orange in color with no evidence of angioedema. No jaundice or other cutaneous signs of liver diseases were noticed. Examination of other parts of the body, including hair, nails and mucous membranes were unremarkable. Skin biopsy was performed along with complete blood count (CBC), peripheral blood film, complete metabolic panel, antinuclear antibody, anti-double stranded DNA antibodies (anti-dsDNA), complements level and hepatitis screening. The biopsy showed dermal edema with inflammatory cells infiltration of the small vessels along with red blood cells extravasation (Figure 2). The diagnosis of urticarial vasculitis was made.



Figure 1 Yellowish plaques with an oedematous erythematous border on the inner aspect of the thighs.

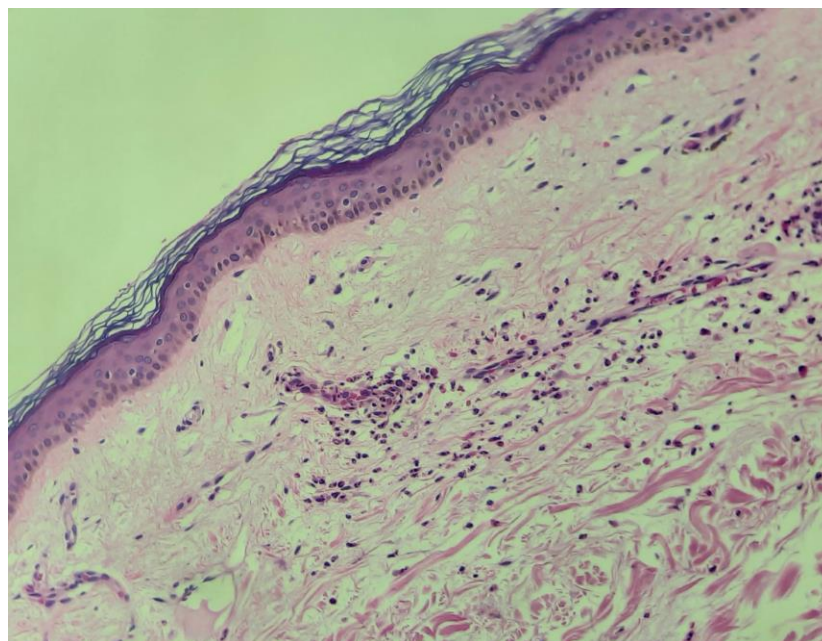


Figure 2 Biopsy showed dermal edema and inflammatory cells infiltration with red blood cells extravasation.

The significant findings in the laboratory investigation were elevation of total and direct bilirubin. Total bilirubin: 45 (3.4-20.5 $\mu\text{mol/L}$) Direct bilirubin: 13.7 (<8.6 $\mu\text{mol/L}$). Abdominal ultrasound examination (US) revealed multiple gallbladder stones with dilatation of the common bile duct. The patient started on Colchicine and referred to gastroenterology clinic for further evaluation of the case.

3. DISCUSSION

Yellow urticaria is an uncommon variant of urticaria and its cause remains unknown (Boechat Souza et al., 2017). The majority of the cases were linked to elevated blood bilirubin levels caused by a variety of liver disorders (Combalia et al., 2017a). The yellow color of the wheels result from the diffuse of excess bilirubin into the surrounding dermis due to increased capillary permeability induced by urticaria (Boechat Souza et al., 2017; Combalia et al., 2017b). The majority of the reported cases were related to chronic liver dysfunction like (end-stage liver disease, metastatic disease of breast and colon, hepatic cirrhosis associated with alcohol, viruses, and hemochromatosis) (Boechat Souza et al., 2017; Çakıcı et al., 2021; Combalia et al., 2017a, 2017b; Imanishi et al., 2006; Koumaki et al., 2021; Narváez-Moreno and Pereyra-Rodríguez, 2012). Other cases were related to biliary pancreatitis, following plasma transfusion, and after the usage of antiretroviral therapy (Mendes et al., 2018; Merdji et al., 2018; Nava Cruz et al., 2017) (Table 1).

Table 1 Literature review of the reported cases of yellow urticaria

Title	Authors	Year of publication	N of cases	Age	Sex	Skin biopsy	Total bilirubin (mg/dl)	Direct bilirubin (mg/dl)	Indirect bilirubin (mg/dl)	Associated disease	Treatment
Yellow Urticaria Secondary to Hyperbilirubinemia in a Patient with End-Stage Liver Disease	(Patel and Mutasim, 2002)	2002	1	48	M	YES	5.4	1.5	3.9	Alcohol-induced end-stage liver disease	Fexofenadine 60 mg twice daily
Yellow urticaria associated with hepatitis type-C liver cirrhosis	(Imanishi et al., 2006)	2006	1	58	M	YES	4.1	3.1	1.0	VHC induced liver cirrhosis	Chlorpheniramine maleate
"Urticaria amarillaporacumulación de bilirrubina" (article in spanish)	(Cabanillas González et al., 2008)	2008	1	68	M	YES	2.8	1.8	1.0	liver cirrhosis	Hidroxycine 25 mg three times daily
Yellow urticaria	(Narváez-Moreno and Pereyra-Rodríguez, 2012)	2012	1	43	F	YES	8.4	7.5	0.9	Metastatic disease to the liver (breast)	Antihistamines (not specified)
Yellow urticaria in a patient with hepatic cirrhosis	(Chiba et al., 2014)	2014	1	56	M	NO	8.1	5.2	2.9	VHC and alcohol-related liver cirrhosis	Not specified
"Un cas d'urticaire jeune" (article in french)	(Benamara-Lévy et al., 2015)	2014	1	65	F	NO	4.8	2.7	2.2	Acute liver failure	Dexchlorpheniramine maleate 10mg once
Yellow urticaria: report of two cases and review of the literature	(Combalia et al., 2017b)	2016	2	1-62 2-58	Both M	1-YES 2-NO	1-7.4 2-7.5	1-2.4 2-2.8	1-5.0 2-4.7	1-Hemochromatosis related liver cirrhosis 2- Alcohol-related liver cirrhosis	1- Dexchlorpheniramine maleate 2mg/12h 2- Ebastine 10mg/8h and topical methylprednisolone aceponat
Yellow Urticaria	(Çakıcı et al., 2021)	2020	2	1-72 2-47	1-F 2-M	Both NO	1-17.4 2-9.98	1-9.12 2-6.52	--	1- cryptogenic cirrhosis and grade 2 hepatic encephalopathy 2- hepatitis B virus-related acute hepatic	1- bilastine 20 mg/d for 3 days 2- intravenous pheniramine maleate twice

										failure	daily
Yellow urticaria and biliary pancreatitis	(Nava Cruz et al., 2017)	2017	1	82	F	YES	5.3	4.0	1.3	biliary pancreatitis and acute cholecystitis	10 mg of loratadine every 12 hours, continued for 30 days
Yellow urticaria in a patient on prophylactic antiretroviral therapy	(Mendes et al., 2018)	2018	1	35	M	NO	7.5	--	7.3	prophylactic antiretroviral therapy after occupational injury with a HIV-positive patient	Fexofenadine (120mg per day)
Cryptogenic cirrhosis: misunderstood cause of yellow urticaria	(Boechat Souza et al., 2017)	2017	1	55	F	NO	--	--	--	cryptogenic cirrhosis	Antihistamines (not specified)
Two cases of yellow urticaria revealing acute lithiasic biliary disease	(Ackerman et al., 2021)	2020	2	1-73 2-66	1-M 2-F	NO	1-2.7 2-3.9	1-2.2 2-2.9	--	1-lithiasic angiocholitis 2-choledochal lithiasis	1-Intravenous dexchlorpheniramine maleate resulted 2-Antihistamines (not specified)
Yellow urticaria following plasma transfusion	(Merdji et al., 2018)	2017	1	55	M	NO	6.9	--	--	alcoholic liver cirrhosis Child C12, (FFP) were administered then yellow urticaria appeared	Antihistamines (not specified)
Yellow urticaria in a patient with alcohol-related liver cirrhosis and jaundice	(Koumaki et al., 2021)	2020	1	61	M	NO	--	13.87	--	acute cholecystitis, alcohol-related liver cirrhosis, and jaundice, drug-induced urticaria	chlorphenamine 4 mg/4 ml iv twice daily for 7 days
"Urticaria amarilla Yellow Urticaria" (article in spanish)	(Segurado Tostón et al., 2021)	2021	1	66	-	NO	--	--	--	metastatic colon adenocarcinoma, peritoneal carcinomatosis, and liver metastases	cetirizine
Present case			1	53	M	YES	2.6	0.8	--	multiple gallbladder stones	topical steroids and oral antihistamine that provided temporary relief

It is also crucial to identify and avoid potential triggers of urticaria. Physical triggers like: (dermographism, cold urticaria, pressure urticaria, solar urticaria, heat urticaria, vibration angioedema, cholinergic urticaria, contact urticaria, and aquagenicurticaria), foods like: (eggs, milk, soy, peanuts in children, fish, shellfish, seafood, and nuts in adults), and medicines likes: (aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme (ACE) inhibitors, codeine, and penicillin) are potential triggers of urticaria. Other causes like infections, smoking, dust, and pollen are all factors to consider. Patients' quality of life will improve greatly if these triggers are avoided. However, it's probable that in our scenario, the high serum bile salt level caused urticaria by activating mast cells and causing them to produce histamine (Ackerman et al., 2021). The differential diagnosis of the case is urticaria, xanthoma, and necrobiotic xanthogranuloma.

Based on the patient's history and clinical signs, a diagnosis of yellow urticarial was made and a biopsy showed dermal edema with inflammatory cells infiltration of the small vessels along with red blood cells extravasation (Figure 2). The diagnosis of urticarial vasculitis was established.

In our case, the patient was prescribed topical steroids and oral antihistamine, which temporarily alleviated the symptoms before they reappeared. Other investigations were ordered to search for the cause of high bilirubin, including US, which showed

multiple gallbladder stones and obstructive jaundice. To conclude, yellow urticaria is a sign of internal disease and it is crucial to be aware of this unusual presentation of urticaria.

4. CONCLUSION

Yellow urticaria is an unusual variant of urticaria with only 15 cases reported in the literature. We have reported a rare case of Yellow urticaria in a patient with hyperbilirubinemia due to gallbladder stones. This case highlights the importance to be vigilant with this unusual presentation of urticaria and, if yellow hives are discovered on clinical examination and no history of jaundice is present, various disorders associated with increased serum bilirubin concentration must be ruled out and search for the triggering factor if any.

Authors' contributions

Moteb K. Alotaibi: Primary author; Abdullah Abdulaziz Abdulwahab Khojah, Asmaa Abdulaziz Abdulwahab Khojah, Hadeel Yousef Alseleem, Maha Abdullah Abdulaziz Binsagr, Mai Ramadan alshammari, Rahaf Faisal Aldawish: All contributed equally to the case report.

Informed Consent

Informed Consent was obtained from the patient.

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Conflict of Interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are presented in the paper.

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